41. (New) The nucleic acid of claim 36, wherein said nucleotide sequence encodes at least 5 contiguous amino acid residues from residues 735-743 of SEQ ID NO:4.

42. (New) The nucleic acid of claim 36, wherein said nucleotide sequence encodes residues 42-215, 221-565, 591-630, 688-731, or 735-743 of SEQ ID NO:4.

43. (New) A kit useful for the detection of an IMPC nucleic acid in a biological sample, comprising one or more nucleic acid of claim 1 or 36.

§3

44. (New) The kit of claim 43, wherein the nucleic acid is a probe.

45. (New) The kit of claim 44, wherein the probe is detectably labeled.--

add 2

REMARKS

Status of the Application; Claim Amendment; and New Claims

Prior to entry of this amendment, claims 1-32 are pending in the application, with claims 4-13 and 18-32 being withdrawn from consideration by the Examiner as directed to non-elected invention, and claims 1-3 and 14-17 being rejected. With entry of this amendment, claims 3, 14-22, and 28-30 have been canceled, claim 1 has been amended, and new claims 33-45 have been added. Thus, claims 1-2 and 33-45 are now pending and under consideration in the application.

Support for the amendment to claim 1 and new dependent claims 33-35 is found throughout the specification, e.g., at pages 34-36, and page 53, lines 3-5. New independent claim 36 and dependent claims 37-42 have support in the specification, e.g., at pages 34-35, and page 53, lines 19-30. Hillier et al. (GenBank Accession No. H38604) and Felbor et al. (GenBank Accession No. AF017772) which are cited in the Office Action report nucleotide sequences that are homologous to SEQ ID NO:3. Applicants note that the Hillier et al. sequence and the Felbor et al. sequence respectively correspond to amino acid residues 379-504 and 431-609 of SEQ ID NO:4, and that they do not disclose a polynucleotide of claims 36-42. New claims 43-45 have support in the specification, e.g., at pages 97-98.

Claim amendment, cancellation of claims, and addition of new claims are made for improved clarity or for purposes of expediting prosecution, and should not be viewed as an acquiescence in any ground of rejection. No new matter has been introduced by the claim amendment and new claims.

With reference to the paragraph numbering in the Office Action, the following remarks address the other issues raised in the Office Action.

1. Sequence Requirements

The Examiner raises issues with the sequences on Figure 5 and page 41 and asks whether they are represented by a SEQ ID NO already in the sequencing listing. In response, Applicants point out that all the sequences shown on page 41 and Figure 5 are represented by the SEQ ID NOs of record. Applicants have accordingly amended the specification to indicate the SEQ ID NOs.

4-5. Claim rejections – 35 U.S.C. § 112, first paragraph, written description

Claims 1-3 and 14-17 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description in the specification. The Examiner says that the claims are directed to and encompass hybridizing sequences and sequences encompassing an IPMC gene, and that none of the sequences as recited by "hybridizing" and "IPMC" gene language meets the written description requirement.

Applicants respectfully disagree with the Examiner's assertion. However, to expedite prosecution, Applicants have amended claim 1 and canceled claims 3 and 14-17. The pending claims after entry of this amendment no longer recite "hybridizing" or "IPMC gene". Accordingly, the instant rejection is moot.

6. Claim rejections under 35 U.S.C. 101

Claims 1-3 and 14-17 are rejected under 35 U.S.C. § 101 as allegedly lacking utility. Specifically, the Examiner says that the nucleic acids being claimed "are purportedly useful in the detection of mutations in an IPMC gene resulting in a susceptibility to a disease", and that "the specification fails to define normal and abnormal IPMC genes and assays for

such detection." The Examiner concludes that "the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility''.

Applicants have canceled claims 14-17 in order to expedite prosecution of the subject application. The new kit claims (claims 43-45) do not contain the language noted above. Therefore, Applicants submit that the instant rejection as applied to claims 14-17 is obviated.

Applicants note that the instant rejection was rendered against both the polynucleotide claims (claims 1-3) and the kits claims (claims 14-17). The basis for the rejection is the alleged lack of teaching in the specification definition of normal and abnormal IMPC genes and assays for detecting mutations in an IPMC gene (see paragraph 6 of the Office Action). Applicants point out that claims 1-3 do not recite normal or abnormal IPMC genes. Thus, the instant rejection is apparently only applicable to claims 14-17.

Further, the presently claimed polynucleotides undoubtedly have a patentable utility. According to the Utility Examination Guidelines issued by the U.S. Patent and Trademark Office on January 5, 2001 (Federal Register 66 (4) 1092-1099):

> An isolated and purified DNA molecule may meet the statutory utility requirement if, e.g., it can be used to produce a useful protein or it hybridizes near and serves as a marker for a disease gene. [see, I. Discussion of Public Comments; PTO response to Comment (8)]

Claims 1-2 and 33-42 recite polynucleotides that comprise the disclosed IPM polynucleotide sequences (or portions thereof) or that encode the disclosed IPM polypeptide sequences (or fragments thereof). The IPM polynucleotides are isolated from the interphotoreceptor matrix (IPM). The interphotoreceptor matrix (IPM) is an extracellular matrix comprised of an array of proteins, glycoproteins, and proteoglycans, occupying the space between the apical surfaces of the neural retina and the RPE. The IPM is important to the maintenance of normal functions of the neural retina, and may play significant roles in both metabolic and hereditary diseases. Applicants have disclosed in the specification isolation and cloning of human IPM cDNAs (e.g., at pages 104 and 110), the full nucleotide sequences of IPM 150 and IPM 200 cDNAs, tissue expression of IPM 150 (e.g., page 122, line 24), and identification and characterization of the IPM 150 and IPM 200 proteins (e.g., page 105). The claimed polynucleotides are useful at least to the extent that they could facilitate production of proteins encoded by the

polynucleotides, that antibodies can be generated against these proteins, and that these agents (proteins, antibodies, primers or probes) can be used to further study diseases that are associated with IPM. Such undoubtedly confers a patentable utility that is substantial, specific, and credible.

In light of the above remarks, Applicants submit that the presently claimed invention has a patentable utility that satisfies the requirement of 35 U.S.C. 101. Withdrawal of the instant rejection is respectfully requested.

7. Claim rejections - 35 U.S.C. § 112, first paragraph, enablement

Claims 1-3 and 14-17 are rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled. The Examiner says that the specification teaches SEQ ID NOs 1, 3, and 5 but "fails to teach normal IPMC genes, abnormal IPMC genes or sequences which can distinguish the aforementioned from each other." The Examiner also says that the skilled artisan "would be forced into further experimentation to determine those sequences which define" a normal or an abnormal IPMC gene and sequences which are capable of distinguishing them, and that the skilled artisan would need undue experimentation to discover those mutations which result in susceptibility to disease. The Examiner concludes that undue experimentation would be required to make and use the claimed invention.

In response, Applicants point out that Claims 14-17 have been canceled in order to expedite prosecution of the subject application. The new kit claims 43-45 do not recite "IPMC gene". Rather, the claims now specifically recite polynucleotides having sequences that are related to the specific IPM sequences disclosed in the specification. The claims also do not recite mutations that result in susceptibility to a disease. With regard to the claims directed to polynucleotides, Applicants note that claims 1-2 and 33-42 do not recite "hybridization". As such, Applicants submit that the pending claims are enabled by the subject specification.

8-10. Claim rejections – 35 U.S.C. § 112, second paragraph

Claims 14-17 are rejected as allegedly being indefinite in the recitation of an "IPMC" gene. Applicants have canceled claims 14-17. Accordingly, the rejection is rendered moot.

11-15 Claim rejections – 35 U.S.C. § 102

12. Claim 1 is rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Strausberg et al. (Genbank Accession No AA815118, March 5, 1998; "Strausberg et al. AA815118"). The Examiner says that Strausberg et al. AA815118 teaches a nucleotide sequence with 100% identity to residues 3213-3426 of SEQ ID NO:5.

To expedite prosecution, Applicants have amended claim 1. With respect to SEQ ID NOs: 5 and 6, the amended claim now recites a polynucleotide comprising a sequence which encodes a polypeptide comprising at least 72 contiguous amino acid residues of SEQ ID NO:6. Strausberg et al. AA815118 only discloses an EST sequence which neither provides an open reading frame nor encodes a polypeptide that comprises at least 72 contiguous amino acid residues of SEQ ID NO:6. Accordingly, Applicants submit that the amended claim 1 and dependent claims 33-35 are novel over Strausberg et al. AA815118.

13. Claim 1 is also rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (Mol. Br. Res. 41:269-78, 1996). The Examiner says that Wang et al. teach nucleic acids with 100% identity to SEQ ID NO:5 residues 3222-3259 of SEQ ID NO:6.

Similarly to Strausberg et al. AA815118, Wang et al. do not disclose a nucleotide sequence that encodes a polypeptide comprising at least 72 contiguous amino acid residues of SEQ ID NO:6. Thus, the claims are also novel over Wang et al.

[Applicants note that two paragraphs in the Office Action are numbered 14. For ease of reference, there are referred to as "14a" and "14b" below]

14a. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Hillier et al. (Genbank Accession No H38604, August 16, 1995). The Examiner

says that "Hillier et al. teach nucleic acids with 99% similarity to nucleic acids 1262-1640 of SEQ ID NO:3 and residues 1262-1573 of SEQ ID NO:5" (Office Action, paragraph 14).

Claim 3 has been canceled. With respect to SEQ ID NO:3, the amended claim 1 now recites polynucleotides comprising a sequence which encodes a polypeptide comprising at least 180 contiguous amino acid residues of SEQ ID NO:4. Hillier et al. report an EST sequence which neither provides an open reading frame nor encodes a polypeptide that comprises at least 180 contiguous amino acid residues of SEQ ID NO:4. Hence, the amended claim 1 and dependent claims 33-35 are novel over Hillier et al.

As to the rejection based on the alleged sequence homology between the Hillier et al. sequence and residues 1262-1573 of SEQ ID NO:5, Applicants note that the sequence alignments attached to the Office Action do not contain an alignment between the Hillier et al. sequence and SEQ ID NO:5. Instead, Applicants could not determine that there is any meaningful sequence homology between the Hillier et al. sequence and residues 1262-1573 of SEQ ID NO:5. In order for Applicants to address this aspect of the instant rejection, clarification by the Examiner is respectfully respected.

14b. Claims 1 and 3 are also rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Felbor et al. (Genbank Accession No AF017772, October 28, 1998) and Cytogenet . Cell Genet. 81:12-17, August 7, 1998. The Examiner says that Felbor et al. teach nucleic acids with 99.6% identity to residues 1416-1954 of SEQ ID NO:3.

Similarly to Hillier et al., Felbor et al. also do not disclose a nucleotide sequence which encodes a polypeptide comprising at least 180 contiguous amino acid residues of SEQ ID NO:4. Thus, the amended claim 1 and dependent claims 33-35 are also novel over Felbor et al.

15. Claim 1 is rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Strausberg et al. (Genbank Accession No AA721009, January 22, 1998; "Strausberg et al. AA721009"). The Examiner says that AA721009 teaches a nucleotide sequence with 100% identity to residues 3223-3426 of SEQ ID NO:5.

Similar to Strausberg et al. AA815118, Strausberg et al. AA721009 also does not disclose an open reading frame or a nucleotide sequence encoding a polypeptide that comprises at least 72 contiguous amino acid residues of SEQ ID NO:6. Accordingly, the pending claims are novel over Strausberg et al. AA721009.

In light of the above claim amendments and remarks, Applicants respectfully request that the rejections under 35 U.S.C. 102 be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400 x 5209.

Respectfully submitted,

Hugh Wang
Reg. No. 47,163

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (650) 326-2400
Fax: (650) 326-2422
PA 3121297 v3